

colon adenocarcinoma, HL-60 acute myelogenous leukemia, Ramos Burkitt lymphoma, and Caki-1 renal cell carcinoma. The cell lines were cultured in the presence of 100 μ M 2-fluorofucose (SGD-2083) in growth media, 100 μ M alkynylfucose (SGD-1887) in growth media, or control growth media (without a fucose analog) for two weeks. The growth media were MEM Eagle with 10% FBS (LS174T), 50:50 F12 and RPMI with 10% FBS (PC-3), RPMI with 10% FBS (HL-60), IMDM with 10% FBS (Ramos), and McCoy with 10% FBS (PC-3). The cells were evaluated for cell surface fucosylation by FACS using antibody cBR96 to detect LewisY, antibody SSEA-1 to detect LewisX, P-selectin ligand to detect P-selectin, and AOL lectin to detect the general level of fucosylation.

Results:

[0216] The results of the FACS evaluation revealed variable levels of fucosylated cell surface proteins on the different cell lines (data not shown). 2-fluorofucose (SGD-2083) was generally a better inhibitor of protein fucosylation than alkynyl fucose (SGD-1887).

Study 2

[0217] To further evaluate the activity of these fucose analogs, further studies were performed in vivo using tumor cells that had been pre-treated by culturing in the presence of a fucose analog, or using untreated tumor cells. Tumor cells were implanted into 10 mice per group as follows. For the LS174-T, PC-3, and Caki-1 cell lines, 5×10^5 cells in 25% Matrigel were implanted subcutaneously into female nude mice. For HL-60 and Ramos cell lines, 5×10^6 cells were implanted subcutaneously into female SCID mice. For mice implanted with untreated tumor cells, mice were provided regular drinking water. For mice implanted with tumor cells pre-treated with 2-fluorofucose (SGD-2083), the mice were provided drinking water supplemented with 20 mM 2-fluorofucose (SGD-2083). For mice implanted with tumor cells pre-treated with alkynyl fucose (SGD-1887), the mice were provided with regular drinking water. The mice did not drink water containing alkynyl fucose.

[0218] After 3 weeks of receiving 2-fluorofucose-containing drinking water, mice were returned to regular drinking water, except for mice with Caki-1 tumors. The latter mice were returned to regular drinking water for one week. After the week of receiving regular water, mice were randomized to two groups of 5 each to receive drinking water supplemented with 20 mM 2-fluorofucose or regular drinking water. Mice were sacrificed when tumors reached about 1000 mm^3 .

[0219] Referring to FIG. 8A-E, tumor growth inhibition in vivo was seen for LS174T, PC-3, and Caki-1 cells treated with 2-fluorofucose (SGD-2083). No change in tumor growth was observed for HL-60 and Ramos cells. For Caki-1, tumor growth inhibition was not observed during the first treatment period, but was observed after the mice were returned to 2-fluorofucose treatment. For the other cell lines, tumor growth inhibition appeared to start when tumor size had reached about 150 mm^3 . The slower growing Caki-1 tumors did not reach this point until the second treatment period with 2-fluorofucose (SGD-2083). These results indicate that treatment with fucose analogs can inhibit tumor growth.

Study 3

[0220] In a third study, tumor cells were implanted without prior treatment with a fucose analog. LS174T colon adenocarcinoma cells (5×10^5 cells in 25% Matrigel) were implanted subcutaneously into female nude mice. Mice were supplied with 50 mM 2-fluorofucose (SGD-2083) in their drinking water from 7 days before implant until 21 days after implant, or were supplied with regular drinking water.

Results

[0221] Referring to FIG. 8F, Mice given 50 mM 2-fluorofucose (SGD-2083) in their drinking water showed a substantial inhibition of tumor growth, achieving an average tumor size of 110 mm^3 versus 734 mm^3 for mice supplied with regular drinking water. Collectively, these results suggest that administration of a fucose analog can inhibit tumor growth.

Example 8

Tumor Vaccine Model

[0222] Female Balb/c mice were immunized by subcutaneous implantation of 1 million A20 murine lymphoma cells (killed by irradiation) on day -21 and day -7. Another group of mice were not given any immunization. On day 0, all mice were inoculated iv with 1.5 or 5 million live A20 cells. On days -14 through +21, mice were provided with 50 mM 2-fluorofucose (SGD-2083) in their drinking water or given regular drinking water. The 8 treatment groups were as follows:

- [0223]** 1. No immunization, 1.5 million live A20 cells, regular drinking water
- [0224]** 2. No immunization, 5 million live A20 cells, regular drinking water
- [0225]** 3. No immunization, 1.5 million live A20 cells, 50 mM SGD-2083 in drinking water
- [0226]** 4. No immunization, 5 million live, A20 cells, 50 mM SGD-2083 in drinking water
- [0227]** 5. Immunized, 1.5 million live A20 cells, regular drinking water
- [0228]** 6. Immunized, 5 million live A20 cells, regular drinking water
- [0229]** 7. Immunized, 1.5 million live A20 cells, 50 mM SGD-2083 in drinking water
- [0230]** 8. Immunized, 5 million live A20 cells, 50 mM SGD-2083 in drinking water

Results

[0231] Referring to FIG. 9A, the study design is shown. Referring to FIG. 9B, mice that did not receive any immunization succumbed to the live A20 challenge from days 22-35. Mice receiving 2-fluorofucose (SGD-2083) survived a few days longer than those receiving regular drinking water. Two mice immunized with 5 million killed A20 cells and receiving regular drinking water succumbed to the live A20 challenge. All mice receiving immunization and 2-fluorofucose (SGD-2083) in their drinking water were still alive at data collection.